

Avenue, 9<sup>th</sup> Floor, Pasadena, California 91101, as directed in the Declaration and Power of Attorney Form filed with the US Patent and Trademark Office on April 2, 2002.

### CONCLUSION

If there are any issues that can be resolved by telephone with the Applicants representative, the Examiner is encouraged to contact the undersigned directly..

The Commissioner is hereby authorized to charge payment of \$434 (\$130 for the one month extension and \$324 for the additional claim fees) to Deposit Account No. 19-2090. The Commissioner is further authorized to charge any other fees or credit any overpayment associated with this Response and Amendment to Deposit Account No. 19-2090.

Respectfully Submitted,

SHELDON & MAK  
a Professional Corporation

Date: 8/21/02

By 

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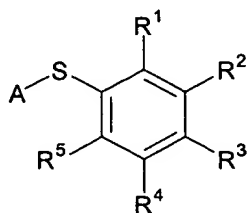
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## SPECIFICATION AMENDMENTS WITH MARKINGS TO SHOW CHANGES

Beginning on page 4, line 8 and ending on page 6, line 14:

The present invention is directed to compounds of [the structure] Formula I

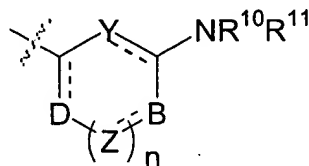


Formula I

or pharmaceutically acceptable salts, optical isomers, or prodrugs thereof,

wherein R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup> and R<sup>5</sup> are each independently selected from the group consisting of hydrogen, halogen, alkyl, haloalkyl, alkoxy, cyano, nitro, cycloalkyl, [and] carboxaldehyde[;], and a group of Formula II defined as:

[with the proviso that at least one of R<sup>1</sup> or R<sup>3</sup> is]



Formula II

subject to the proviso that one or more than one of R<sup>1</sup> or R<sup>3</sup> is a group of  
Formula II as defined above;

wherein D, B, Y and Z at each occurrence are independently selected from the group consisting of -CR<sup>6</sup>=, -CR<sup>7</sup>R<sup>8</sup>-, C(O)-, -O-, -SO<sub>2</sub>-, -S-, -N=, and -NR<sup>9</sup>-;

n is an integer of zero to three;

R<sup>6</sup>, R<sup>7</sup>, R<sup>8</sup>, and R<sup>9</sup>, at each occurrence, are each independently selected from the group consisting of hydrogen, alkyl, carboxy, hydroxyalkyl, alkylaminocarbonyl[alkyl, dialkylaminocarbonylalkyl and carboxyalkyl; and

R<sup>10</sup> and R<sup>11</sup> are each independently selected from the group consisting of hydrogen, alkyl, cycloalkyl, alkoxyalkyl, alkoxycarbonylalkyl, carboxyalkyl, hydroxyalkyl, heterocyclyl, heterocyclylalkyl and heterocyclylamino; or

[wherein] R<sup>10</sup> and R<sup>11</sup> are taken together with N [may be joined] to form a three to seven membered unsubstituted heterocyclyl ring, or a three to seven membered substituted heterocyclyl ring, [said ring being optionally] substituted with one or more than one substituent [substituents] R<sup>13</sup>, wherein R<sup>13</sup>, at each occurrence is independently selected from the group consisting of alkyl, alkylene, alkoxy, alkoxyalkyl, cycloalkyl, aryl, heterocyclyl, heterocyclylalkyl, heterocyclylcarbonyl, heterocyclylalkylaminocarbonyl, hydroxy, hydroxyalkyl, hydroxyalkoxyalkyl, carboxy, carboxyalkyl, carboxycarbonyl, carboxaldehyde, alkoxycarbonyl, arylalkoxycarbonyl, aminoalkyl, aminoalkanoyl, aminocarbonyl, carboxamido, alkoxycarbonylalkyl, carboxamidoalkyl, cyano, tetrazolyl, alkanoyl, hydroxyalkanoyl, alkanoyloxy, alkanoylamino, alkanoyloxyalkyl, alkanoylaminoalkyl, sulfonate, alkylsulfonyl, alkylsulfonylaminocarbonyl, arylsulfonylaminocarbonyl and heterocyclylsulfonylaminocarbonyl;

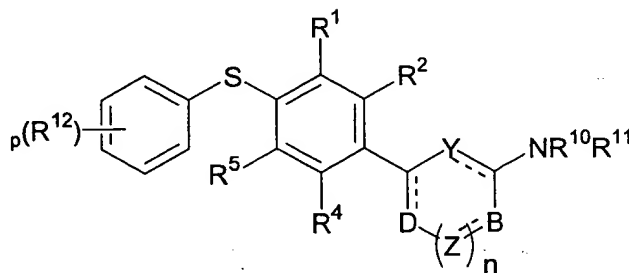
wherein A is an unsubstituted aryl [or] group, an unsubstituted heterocyclyl group, a substituted aryl group, or a substituted heterocyclyl group, substituted with one or more than [said aryl or heterocyclyl group having at least] one substituent R<sup>12</sup>, wherein R<sup>12</sup>, at each occurrence, is independently selected from the group consisting of [hydrogen,] halogen, alkyl, aryl, haloalkyl, hydroxy, alkoxy, alkoxyalkyl, alkoxycarbonyl, alkoxyalkoxy, hydroxyalkyl, aminoalkyl, aminocarbonyl, alkyl(alkoxycarbonylalkyl) aminoalkyl, heterocyclyl,

heterocyclalkyl, carboxaldehyde, carboxaldehyde hydrazone, carboxamide, alkoxycarbonylalkyl, carboxy, carboxyalkyl, carboxyalkoxy, carboxythioalkoxy, carboxycycloalkoxy, thioalkoxy, carboxyalkylamino, trans-cinnamyl, hydroxyalkylaminocarbonyl, cyano, amino, heterocyclalkylamino, and heterocyclalkylaminocarbonyl; and

wherein  $R^1$ ,  $R^2$ ,  $R^3$ ,  $R^4$ ,  $R^5$ ,  $R^6$ ,  $R^7$ ,  $R^8$ ,  $R^9$ ,  $R^{10}$ ,  $R^{11}$ ,  $R^{12}$  and  $R^{13}$  are unsubstituted or substituted with at least one electron donating or electron withdrawing group; [or a pharmaceutically-acceptable salt, optical isomer or prodrug thereof].

Beginning on page 6, line 18 and ending on page 8, line 16:

The present invention is also directed to compounds of [the structure] Formula III



Formula III

wherein  $R^1$ ,  $R^2$ ,  $R^3$ ,  $R^4$  and  $R^5$  are each independently selected from the group consisting of hydrogen, halogen, alkyl, haloalkyl, alkoxy, cyano, nitro, cycloalkyl and carboxaldehyde;

D, B, Y and Z are as defined above for Formula I;

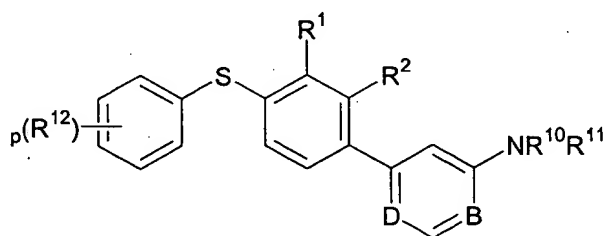
$R^{12}$ , at each occurrence, is independently selected from the group consisting of [hydrogen,] halogen, alkyl, haloalkyl, alkoxy, carboxyalkoxy, carboxyalkyl and heterocycl; and[,]

p is an integer of zero to five;

wherein  $R^1$ ,  $R^2$ ,  $R^4$ ,  $R^5$ ,  $R^{10}$ ,  $R^{11}$  and  $R^{12}$  are unsubstituted or substituted with at least one electron donating group or electron withdrawing group.

Presently most preferred, but not required, compounds of Formula III have  $p$  as one;  $R^4$  and  $R^5$  as hydrogen;  $R^{12}$  as halogen, alkyl, carboxyalkoxy, carboxyalkyl or heterocyclyl; and  $R^{10}$  and  $R^{11}$  [joined] are taken together with N to form a three to seven membered unsubstituted heterocyclyl ring, or a three to seven membered substituted heterocyclyl ring; said ring being piperidine, piperazine, morpholine, pyrrolidine or azetidine.

Presently most preferred, but not required, compounds are of [the structure] Formula IV



Formula IV

wherein D and B are each independently selected from the group consisting of  $-N=$  and  $-CR^6=$ ;

$R^1$  and  $R^2$  are each independently selected from the group consisting of hydrogen, halogen and haloalkyl;

$R^{10}$  and  $R^{11}$  are as defined above for Formula I;

$R^{12}$ , at each occurrence, is independently selected from the group consisting of [hydrogen], halogen, alkyl, haloalkyl, alkoxy, carboxyalkoxy, carboxyalkyl and heterocyclyl;

$p$  is an integer of zero to five; and[,]

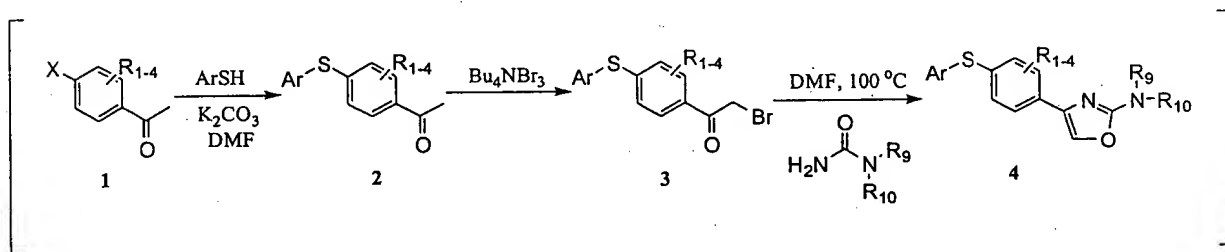
wherein  $R^1$ ,  $R^2$ ,  $R^{10}$ ,  $R^{11}$ , and  $R^{12}$  are unsubstituted or substituted with at least one electron donating group or electron withdrawing group.

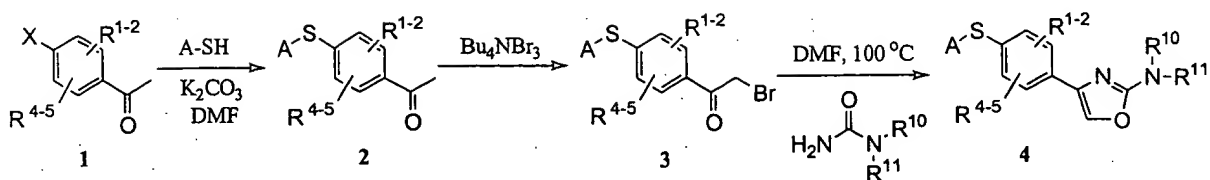
[For presently] Presently most preferred, but not required, compounds are of Formula IV, where p [may] can be one;  $R^{12}$  [may] can be halogen, alkyl, alkoxy, carboxyalkoxy, carboxyalkyl or heterocyclyl; and  $R^{10}$  and  $R^{11}$  [may] can be [joined] taken together with N to form a three to seven membered heterocyclyl ring; said ring being piperidine, piperazine, morpholine, pyrrolidine or azetidine.

Beginning on page 28, line 10 (with the words "Scheme I"), and ending on page 31, line 10:

Scheme [I] 1 describes compounds of Formula I which contain an oxazole ring ( $n=0$ ,  $Y=N$ ,  $B=O$ ,  $D=C$ ). In Scheme 1, and likewise in Schemes 2 and 4, the substituent X is a leaving group. In Scheme I, aryl [Aryl] methyl ketone 1, with [the] an appropriate substitution ( $R_{1-2}$  and  $R_{4-5}$ ), and a leaving group  $X$ , reacts with an aryl thiol to give a biaryl sulfide 2. Biarylsulfide 2 can be converted into an alpha-bromomethyl ketone 3 using a variety of reagents including  $Bu_4NBr_3$ . Condensation of 3 with a urea [then] gives a [the] desired [compounds] oxazole compound 4.

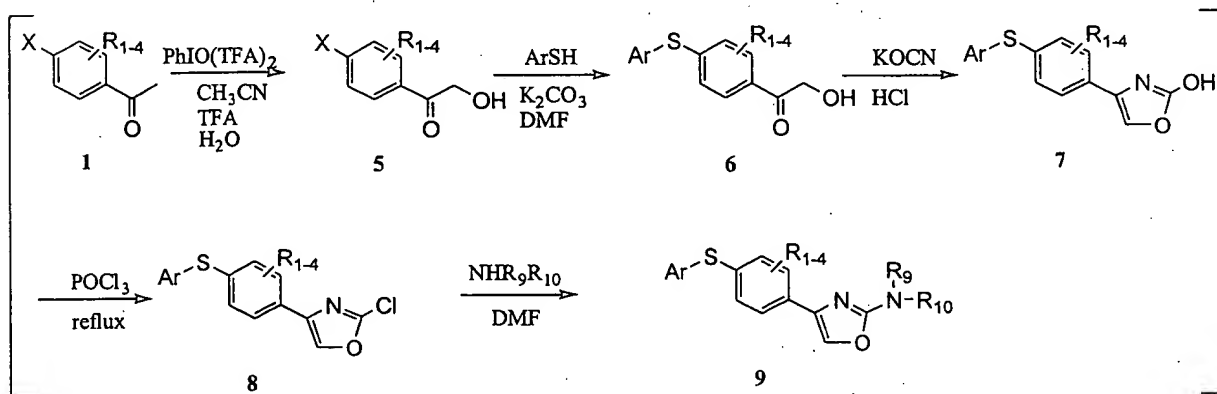
Scheme 1

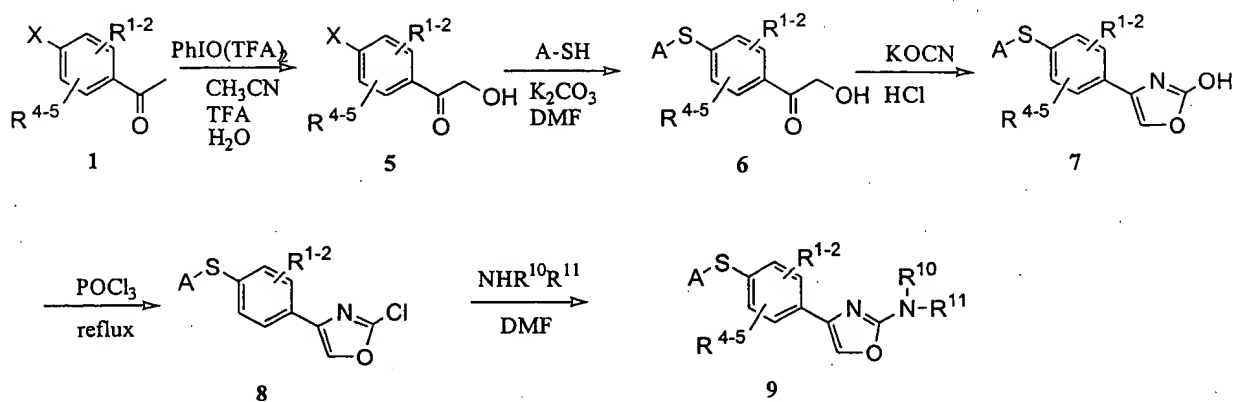




Another method of preparing compounds of Formula I containing an oxazole ring ( $n=0$ ,  $Y=N$ ,  $B=O$ ,  $D=C$ ) is illustrated in Scheme 2. In Scheme 2, an aryl [Aryl] methyl ketone [ketones] 1 is [1 are] converted into an alpha-hydroxymethyl ketone 5, which then can be reacted with an arylthiol [arylthiols] to give a biaryl sulfide 6. Acid-catalyzed condensation of 6 with KOCN affords a 2-hydroxy oxazole 7, which can be converted into a 2-chloro-oxazole 8 using  $POCl_3$ . Displacement of the chloride of 8 with an amine [amines] gives a [the] desired 2-amino-oxazole 9.

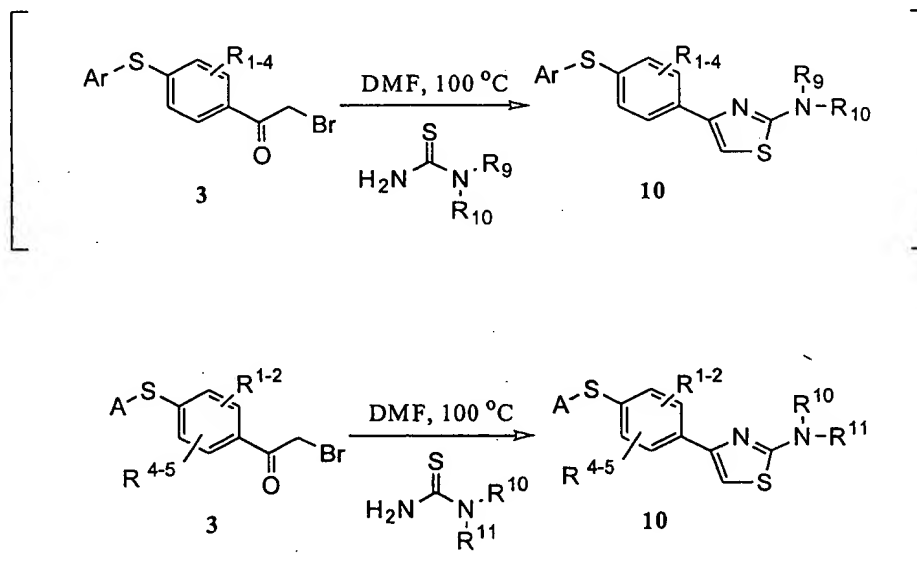
Scheme 2





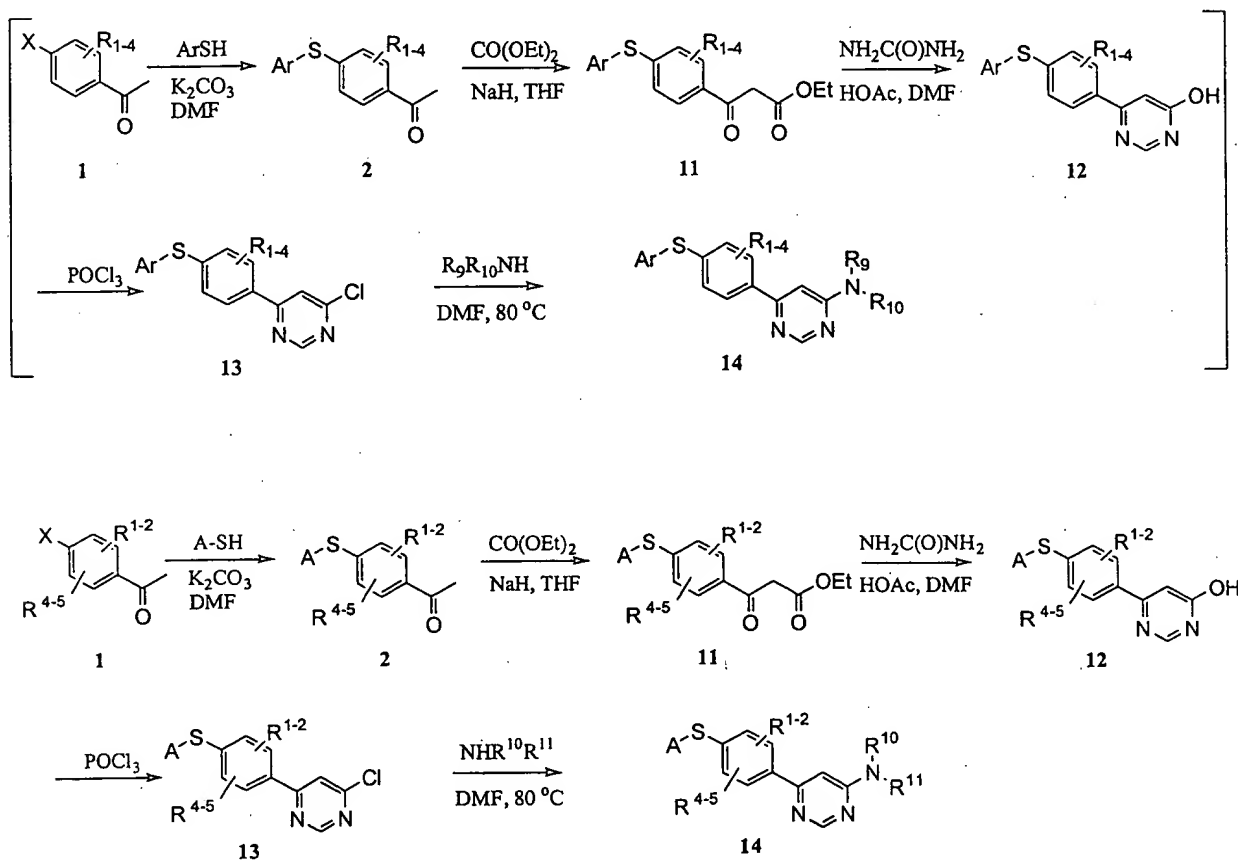
Scheme 3 describes the synthesis of a class of compounds of Formula I containing a thioazole ring ( $n=0$ ,  $Y=N$ ,  $B=S$ ,  $D=C$ ). In Scheme 3, [The] biaryl sulfide alpha-bromomethyl ketone 3 can be prepared following the procedure outline in Scheme 1. Condensation of 3 with a properly substituted thiourea gives a [the] desired 2-aminothioazole 10.

Scheme 3



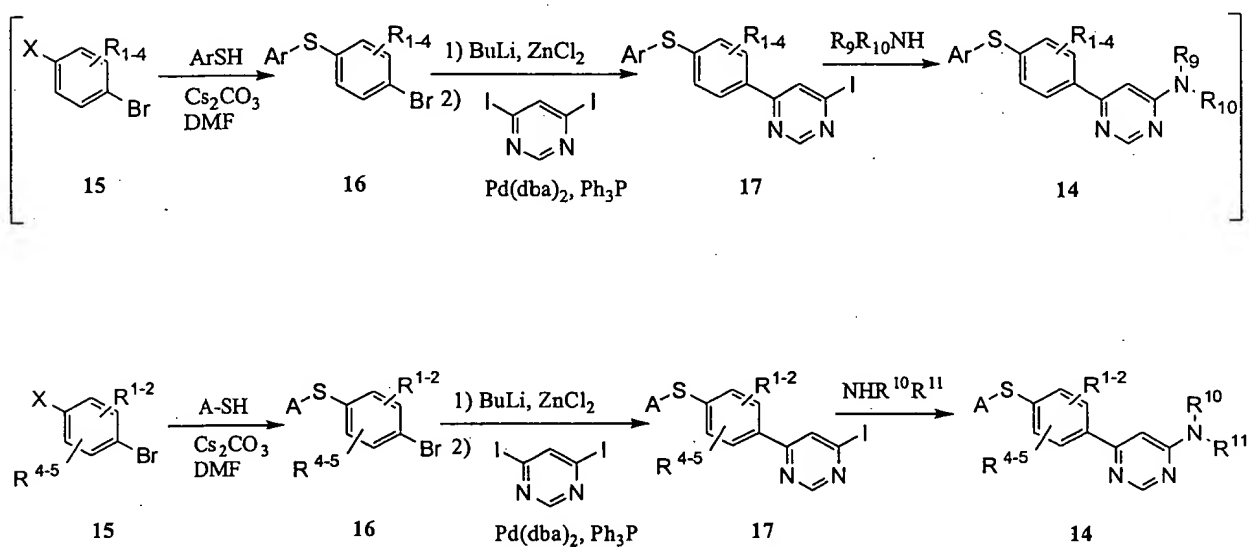
Another class of compounds of Formula I are compounds containing pyrimidine ring, for example 4,6-disubstituted pyrimidines ( $n=1$ ,  $Y=C$ ,  $B=N$ ,  $Z=C$ ,  $D=N$ ). Scheme 4 describes one procedure for the preparation of this class of compounds. Reaction of a biaryl sulfide methyl ketone **2** with diethyl carbonate under base-catalysis leads to a  $\beta$ -ketoester **11**. Condensation of **11** with formamidine gives a 4-hydroxy pyrimidine **12**, which can be converted into 4-chloropyrimidine **13**. Displacement of the chloride of **13** by amines then gives the desired 4-amino-pyrimidine **14**.

Scheme 4



An alternative synthesis of the 4,6-disubstituted pyrimidines is illustrated in Scheme 5. In Scheme 5, nucleophilic [Nucleophilic] substitution of an aryl fluoride 15 with an aryl thio under base-catalysis gives a biaryl sulfide 16. Transmetalation of 16 with n-BuLi/ZnCl<sub>2</sub>, followed by Pd-catalyzed cross-coupling with 4,6-diiodopyrimidine leads to iodopyrimidine 17. Reaction of 17 with a selected amine [amines] gives a [the] desired 4-aminopyrimidine 14.

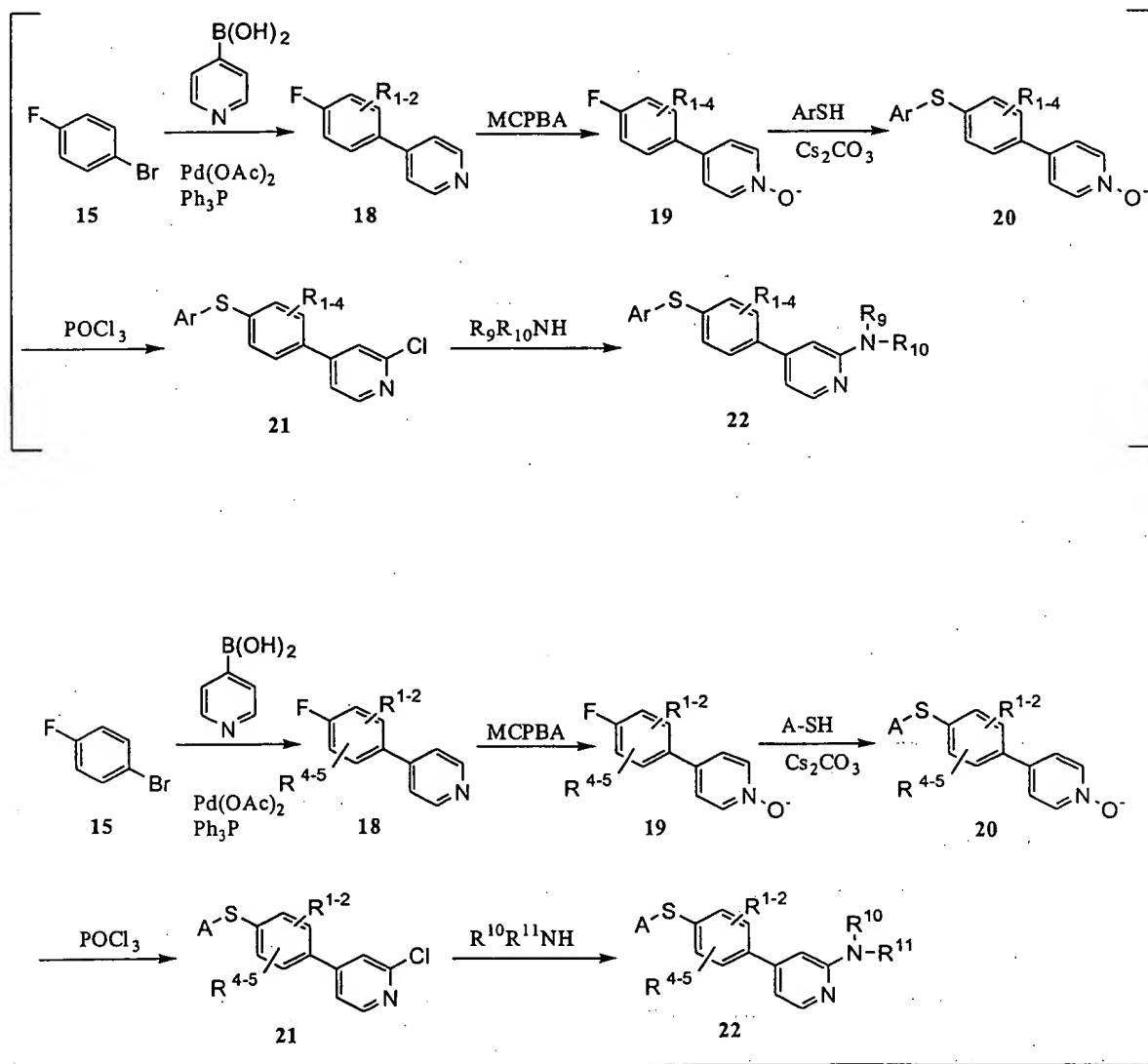
Scheme 5



Yet another class of compounds of Formula I are compounds containing a pyridine ring, for example 2,4-disubstituted pyridines ( $n=1$ ,  $Y=C$ ,  $B=N$ ,  $Z=C$ ,  $D=C$ ). Scheme 6 describes one procedure for the preparation of this class of compounds. In Scheme 6, [Thus,] Pd-catalyzed cross-coupling of a properly substituted 1-bromo-4-fluoro-benzene 15 and 4-pyridine boronic acid gives compounds 18. Oxidation of 18 with MCPBA leads to pyridinium oxide 19. Displacement of the fluoride of 19 with an aryl thio [thiols then] affords biarylsulfide 20. Treatment of 20 with POCl<sub>3</sub>, leads to 2-chloropyridine 21. Finally, reaction

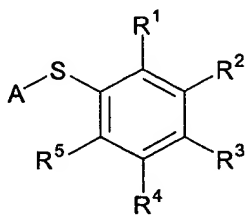
of 21 with a selected amine [amines] gives a [the] desired 2-aminopyridine [2-aminopyridines] 22.

Scheme 6



## VERSION OF AMENDED CLAIMS WITH MARKINGS TO SHOW CHANGES

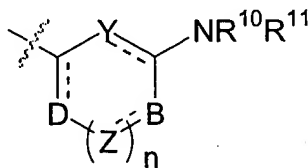
1. (Amended) A compound of [the structure] formula I



I

or a pharmaceutically acceptable salt or prodrug thereof.

wherein R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup> and R<sup>5</sup> are each independently selected from the group consisting of hydrogen, halogen, alkyl, haloalkyl, alkoxy, cyano, nitro, cycloalkyl, [and] carboxaldehyde[;], and a group of formula II defined as



II

subject to [with] the proviso that one or more than [at least] one of R<sup>1</sup> or R<sup>3</sup> is a group of formula II as defined above;

wherein D, B, Y and Z at each occurrence are independently selected from the group consisting of -CR<sup>6</sup>=, -CR<sup>7</sup>R<sup>8</sup>-, C(O)-, -O-, -SO<sub>2</sub>-, -S-, -N=, and -NR<sup>9</sup>-;

n is an integer of zero to three;

R<sup>6</sup>, R<sup>7</sup>, R<sup>8</sup>, and R<sup>9</sup>, at each occurrence, are each independently selected from the group consisting of hydrogen, alkyl, carboxy, hydroxyalkyl, alkylaminocarbonyl[alkyl, dialkylaminocarbonylalkyl and carboxyalkyl; and

R<sup>10</sup> and R<sup>11</sup> are each independently selected from the group consisting of hydrogen, alkyl, cycloalkyl, alkoxyalkyl, alkoxycarbonylalkyl, carboxyalkyl, hydroxyalkyl, heterocyclyl, heterocyclylalkyl and heterocyclylamino; or [wherein] R<sup>10</sup> and R<sup>11</sup> are taken together with N [may be joined] to form a three to seven membered unsubstituted heterocyclyl ring, or a three to seven membered substituted heterocyclyl ring, [said ring being optionally] substituted with one or more than one substituent [substituents] R<sup>13</sup>, wherein R<sup>13</sup>, at each occurrence is independently selected from the group consisting of alkyl, alkylene, alkoxy, alkoxyalkyl, cycloalkyl, aryl, heterocyclyl, heterocyclylalkyl, heterocyclylcarbonyl, heterocyclylalkylaminocarbonyl, hydroxy, hydroxyalkyl, hydroxyalkoxyalkyl, carboxy, carboxyalkyl, carboxycarbonyl, carboxaldehyde, alkoxycarbonyl, arylalkoxycarbonyl, aminoalkyl, aminoalkanoyl, aminocarbonyl, carboxamido, alkoxycarbonylalkyl, carboxamidoalkyl, cyano, tetrazolyl, alkanoyl, hydroxyalkanoyl, alkanoyloxy, alkanoylamino, alkanoyloxyalkyl, alkanoylaminoalkyl, sulfonate, alkylsulfonyl, alkylsulfonylaminocarbonyl, arylsulfonylaminocarbonyl and heterocyclylsulfonylaminocarbonyl;

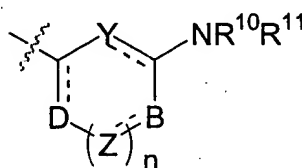
wherein A is an unsubstituted aryl [or] group, an unsubstituted heterocyclyl group, a substituted aryl group, or a substituted heterocyclyl group, substituted with one or more than [said aryl or heterocyclyl group having at least] one substituent R<sup>12</sup>, wherein R<sup>12</sup>, at each occurrence, is independently selected from the group consisting of [hydrogen,] halogen, alkyl, aryl, haloalkyl, hydroxy, alkoxy, alkoxyalkyl, alkoxycarbonyl, alkoxyalkoxy, hydroxyalkyl, aminoalkyl, aminocarbonyl, alkyl(alkoxycarbonylalkyl) aminoalkyl, heterocyclyl, heterocyclylalkyl, carboxaldehyde, carboxaldehyde hydrazone, carboxamido, alkoxycarbonylalkyl, carboxy, carboxyalkyl, carboxyalkoxy, hydroxyalkylaminocarbonyl, cyano, amino, heterocyclylalkylamino,

carboxythioalkoxy, carboxycycloalkoxy, thioalkoxy, carboxyalkylamino, trans-cinnamyl and heterocyclylalkylaminocarbonyl; and

wherein  $R^1$ ,  $R^2$ ,  $R^3$ ,  $R^4$ ,  $R^5$ ,  $R^6$ ,  $R^7$ ,  $R^8$ ,  $R^9$ ,  $R^{10}$ ,  $R^{11}$ ,  $R^{12}$  and  $R^{13}$  are unsubstituted or substituted with one or more than [at least] one electron donating or electron withdrawing group[;]

[or a pharmaceutically-acceptable salt, optical isomer or prodrug thereof].

2. A [The] compound according to [of] claim 1 wherein  $R^3$  is the group of formula II



II

wherein  $R^{10}$ ,  $R^{11}$ , D, B, Y, [and] Z, and n are defined as in claim 1. [at each occurrence are defined as in claim 1 independently selected from the group consisting of  $-CR^6=$ ,  $-CR^7R^8-$ ,  $C(O)-$ ,  $-O-$ ,  $-SO_2-$ ,  $-S-$ ,  $-N=$ , and  $-NR^9-$ ;

n is an integer of zero to three;

$R^6$ ,  $R^7$ ,  $R^8$ , and  $R^9$ , at each occurrence, are each independently selected from the group consisting of hydrogen, alkyl, carboxy, hydroxyalkyl, alkylaminocarbonylalkyl, dialkylaminocarbonylalkyl and carboxyalkyl;

$R^{10}$  and  $R^{11}$  are each independently selected from the group consisting of hydrogen, alkyl, cycloalkyl, alkoxyalkyl, alkoxycarbonylalkyl, carboxyalkyl, hydroxyalkyl, heterocyclyl, heterocyclylalkyl and heterocyclylamino;

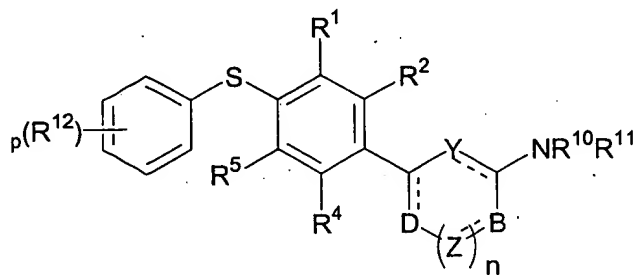
$R^{10}$  and  $R^{11}$  may be joined to form a three to seven membered heterocyclyl ring, substituted with one or more substituents  $R^{13}$ , wherein  $R^{13}$ , at each occurrence is independently selected from the group consisting of alkyl, alkylene, alkoxy,

alkoxyalkyl, cycloalkyl, aryl, heterocyclyl, heterocyclylalkyl, heterocyclylcarbonyl, heterocyclylalkylaminocarbonyl, hydroxy, hydroxyalkyl, hydroxyalkoxyalkyl, carboxy, carboxyalkyl, carboxycarbonyl, carboxaldehyde, alkoxycarbonyl, arylalkoxycarbonyl, aminoalkyl, aminoalkanoyl, aminocarbonyl, carboxamido, alkoxycarbonylalkyl, carboxamidoalkyl, cyano, tetrazolyl, alkanoyl, hydroxyalkanoyl, alkanoyloxy, alkanoylamino, alkanoyloxyalkyl, alkanoylaminoalkyl, sulfonate, alkylsulfonyl, alkylsulfonylaminocarbonyl, arylsulfonylaminocarbonyl and heterocyclylsulfonylaminocarbonyl;

R<sup>1</sup> and R<sup>2</sup> are each independently selected from the group consisting of hydrogen, halogen, haloalkyl and nitro; and

R<sup>4</sup> and R<sup>5</sup> are each independently selected from the group of hydrogen and alkyl.]

3. (Amended) A [The] compound according to [of] claim 1 of [the structure] formula III



III

wherein R<sup>1</sup>, R<sup>2</sup>, R<sup>4</sup>, R<sup>5</sup>, R<sup>10</sup>, R<sup>11</sup>, R<sup>12</sup>, D, B, Y, Z, and n are defined as in claim 1;

[R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup> and R<sup>5</sup> are each independently selected from the group consisting of hydrogen, halogen, alkyl, haloalkyl, alkoxy, cyano, nitro, cycloalkyl and carboxaldehyde;

wherein D, B, Y and Z at each occurrence are independently selected from the group

consisting of  $-\text{CR}^6=$ ,  $-\text{CR}^7\text{R}^8-$ ,  $\text{C}(\text{O})-$ ,  $-\text{O}-$ ,  $-\text{SO}_2-$ ,  $-\text{S}-$ ,  $-\text{N}=\text{}$ , and  $-\text{NR}^9-$ ;

$n$  is an integer of zero to three;

wherein  $\text{R}^6$ ,  $\text{R}^7$ ,  $\text{R}^8$ , and  $\text{R}^9$ , at each occurrence, are each independently selected from the group consisting of hydrogen, alkyl, carboxy, hydroxyalkyl, alkylaminocarbonyl alkyl, dialkylaminocarbonylalkyl and carboxyalkyl;

$\text{R}^{10}$  and  $\text{R}^{11}$  are each independently selected from the group consisting of hydrogen, alkyl, cycloalkyl, alkoxyalkyl, alkoxycarbonylalkyl, carboxyalkyl, hydroxyalkyl, heterocyclyl, heterocyclylalkyl and heterocyclylamino;

wherein  $\text{R}^{10}$  and  $\text{R}^{11}$  may be joined to form a three to seven membered heterocyclyl ring, substituted with one or more substituents  $\text{R}^{13}$ , wherein  $\text{R}^{13}$ , at each occurrence is independently selected from the group consisting of alkyl, alkylene, alkoxy, alkoxyalkyl, cycloalkyl, aryl, heterocyclyl, heterocyclylalkyl, heterocyclylcarbonyl, heterocyclylalkylaminocarbonyl, hydroxy, hydroxyalkyl, hydroxyalkoxyalkyl, carboxy, carboxyalkyl, carboxycarbonyl, carboxaldehyde, alkoxycarbonyl, arylalkoxycarbonyl, aminoalkyl, aminoalkanoyl, aminocarbonyl, carboxamido, alkoxycarbonylalkyl, carboxamidalkyl, cyano, tetrazolyl, alkanoyl, hydroxyalkanoyl, alkanoyloxy, alkanoylamino, alkanoyloxyalkyl, alkanoylaminoalkyl, sulfonate, alkylsulfonate, alkylsulfonaminocarbonyl, arylsulfonaminocarbonyl and heterocyclylsulfonaminocarbonyl;

$\text{R}^{12}$ , at each occurrence, is independently selected from the group consisting of hydrogen, halogen, alkyl, haloalkyl, alkoxy, carboxyalkoxy, carboxyalkyl and heterocyclyl;] and

$p$  is an integer of zero to five[;

wherein  $\text{R}^1$ ,  $\text{R}^2$ ,  $\text{R}^4$ ,  $\text{R}^5$ ,  $\text{R}^{10}$ ,  $\text{R}^{11}$ ,  $\text{R}^{12}$ , and  $\text{R}^{13}$  are unsubstituted or substituted with at least one electron donating or electron withdrawing group].

4. (Amended) A [The] compound according to [of] claim 3 wherein p is one;

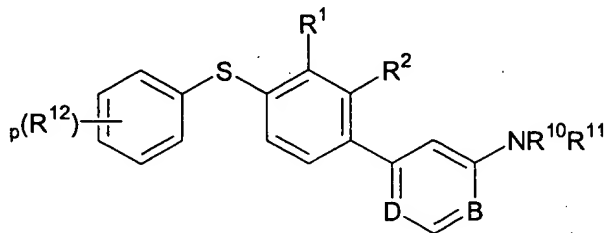
$R^4$  and  $R^5$  are hydrogen;

$R^{12}$  is selected from the group consisting of halogen, alkyl, alkoxy, carboxyalkoxy, carboxyalkyl and heterocyclyl;

$R^{10}$  and  $R^{11}$  are taken together with N [joined] to form a three to seven membered unsubstituted heterocyclyl ring, or a three to seven membered substituted heterocyclyl ring[;], substituted with one or more than one substituent [substituents]  $R^{13}$ , wherein  $R^{13}$  is defined as in claim 1, and wherein said substituted heterocyclyl, or unsubstituted heterocyclyl ring is selected from the group consisting of piperidine, piperazine, morpholine, pyrrolidine, and azetidine[.]; and

wherein  $R^{10}$ ,  $R^{11}$ ,  $R^{12}$  and  $R^{13}$  are unsubstituted or substituted with at least one electron donating or electron withdrawing group.

5. (Amended) A [The] compound according to [of] claim 1 of [the structure] formula IV



IV

wherein D and B are each independently selected from the group consisting of  $-N=$  and  $-CR^6=$ ;

$R^1$  and  $R^2$  are each independently selected from the group consisting of hydrogen, halogen and haloalkyl;

$R^{10}$  and  $R^{11}$  are defined as in claim 1;

[R<sup>10</sup> and R<sup>11</sup> are each independently selected from the group consisting of hydrogen, alkyl, cycloalkyl, alkoxyalkyl, alkoxycarbonylalkyl, carboxyalkyl, hydroxyalkyl, heterocyclyl, heterocyclylalkyl and heterocyclylamino;

wherein R<sup>10</sup> and R<sup>11</sup> may be joined to form a three to seven membered heterocyclyl ring, substituted with one or more substituents R<sup>13</sup>, wherein R<sup>13</sup>, at each occurrence is independently selected from the group consisting of alkyl, alkylene, alkoxy, alkoxyalkyl, cycloalkyl, aryl, heterocyclyl, heterocyclylalkyl, heterocyclylcarbonyl, heterocyclylalkylaminocarbonyl, hydroxy, hydroxyalkyl, hydroxyalkoxyalkyl, carboxy, carboxyalkyl, carboxycarbonyl, carboxaldehyde, alkoxycarbonyl, arylalkoxycarbonyl, aminoalkyl, aminoalkanoyl, aminocarbonyl, carboxamido, alkoxycarbonylalkyl, carboxamidoalkyl, cyano, tetrazolyl, alkanoyl, hydroxyalkanoyl, alkanoyloxy, alkanoylamino, alkanoyloxyalkyl, alkanoylaminoalkyl, sulfonate, alkylsulfonyl, alkylsulfonylaminocarbonyl, arylsulfonylaminocarbonyl and heterocyclylsulfonylaminocarbonyl;]

R<sup>12</sup>, at each occurrence, is independently selected from the group consisting of [hydrogen,] halogen, alkyl, haloalkyl, alkoxy, carboxyalkoxy, carboxyalkyl and heterocyclyl, wherein R<sup>12</sup> is unsubstituted or substituted with at least one electron donating group or electron withdrawing group; and[,]

p is an integer of zero to five[;

[wherein R<sup>1</sup>, R<sup>2</sup>, R<sup>10</sup>, R<sup>11</sup>, R<sup>12</sup> and R<sup>13</sup> are unsubstituted or substituted with at least one electron donating group or electron withdrawing group].

6. (Amended) A [The] compound according to [of] claim 5 wherein p is one;

[R<sup>12</sup> is selected from the group consisting of halogen, alkyl, alkoxy, carboxyalkoxy, carboxyalkyl and heterocyclyl;] and

R<sup>10</sup> and R<sup>11</sup> are taken together with N [joined] to form a three to seven membered

substituted heterocyclyl ring, or a three to seven membered unsubstituted heterocyclyl ring[;], substituted with one or more substituents R<sup>13</sup>, wherein R<sup>13</sup> is defined as in claim 1, and wherein said substituted heterocyclyl ring, or unsubstituted heterocyclyl ring is selected from the group consisting of piperidine, piperazine, morpholine, pyrrolidine, and azetidine.

7. (Amended) A [The] compound according to [of] claim 1 selected from the group consisting of 1-(6-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyrimidin-4-yl)-piperidine-3-carboxylic acid, 4-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-6-(3-(2*H*-tetrazol-5-yl)-piperidin-1-yl)-pyrimidine, 4-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-6-(4-(2*H*-tetrazol-5-yl)-piperidin-1-yl)-pyrimidine, (1-(6-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyrimidin-4-yl)-piperidin-3-yl)-methanol, 2-(1-(6-(4-(2-isopropylphenylsulfanyl)-3-trifluoromethyl-phenyl)-pyrimidin-4-yl)-piperidin-4-yl)-ethanol, *N*-(1-(4-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyridin-2-yl)-pyrrolidin-3-yl)-acetamide, 1-(4-(4-(2-methoxy-phenylsulfanyl)-3-trifluoromethyl-phenyl)pyridin-2-yl)-pyrrolidine-3-ol, *N*-1-(4-(4-(2-methoxy-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyridin-2-yl)-pyrrolidine-3-yl)-acetamide, *N*-1-(4-(4-(2-methoxy-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyridin-2-yl)-pyrrolidine-3-yl)-acedemide, *N*-1-(4-(4-(2-methoxy-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyridin-2-yl)-pyrrolidin-3-yl)-acetamide, 4'-(4-(2,3-dihydro-benzo(1,4)dioxin-6-ylsulfanyl)-3-trifluoromethyl-phenyl)- 3,4, 5, 6 -tetrahydro-2*H*-(1,2') bipyridinyl-4-carboxylic acid, and 4'-(4-(2,3-dihydrobenzo (1,4) dioxin-6-ylsulfanyl)-3-trifluoromethyl-phenyl)-3,4,5,6-tetrahydro-2*H*-(1,2')(bipyridinyl-3-carboxylic acid.

8. (Amended) A composition comprising:

a compound according to [of] claim 1

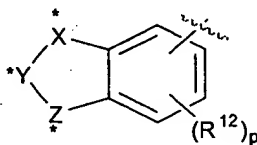
and [in] a pharmaceutically acceptable carrier.

9. (Amended) A method of inhibiting inflammation or suppressing immune response in a mammal comprising administering to said mammal a therapeutic amount of a compound

according to [of] claim 1.

10. (New) A compound according to claim 1 wherein A is

- (i) an unsubstituted or substituted aryl group, substituted by one or more than one substituent  $R^{12}$ , wherein  $R^{12}$  is defined as in claim 1, or
- (ii) an unsubstituted or substituted heterocyclyl group of the formula



wherein

$R^{12}$  and is defined as in claim 1;

p is an integer of 0 to 5;

$X^*$  and  $Z^*$  are each independently selected from the group consisting of  $-CH_2-$ ,  $-CH_2NH-$ ,  $-CH_2O-$ ,  $-NH-$ , and  $-O-$ , with the proviso that at least one of  $X^*$  and  $Z^*$  is not  $-CH_2-$ ; and

$Y^*$  is  $-(C(R''))_v-$ , wherein

$R''$  is hydrogen or alkyl; and

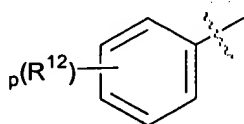
v is 1, 2, or 3.

11. (New) A compound according to claim 1 or 10 wherein A is an unsubstituted or substituted aryl group, wherein the aryl group is

- a) a mono- or a bicyclic carbocyclic ring system having one or two aromatic rings, or
- b) a mono- or a bicyclic carbocyclic ring system having one or two aromatic rings, wherein one or more than one of the aromatic rings is fused to a ring selected

from the group consisting of cyclohexane, cyclohexene, cyclopentane, and cyclopentene.

12. (New) A compound according to claim 1 wherein A is an unsubstituted or substituted aryl group of the formula



wherein  $R^{12}$  is defined as in claim 1; and  $p$  is an integer of 0 to 5.

13. (New) A compound according to claim 1 wherein

D is  $-CR^6=$  or  $-N=$ ,

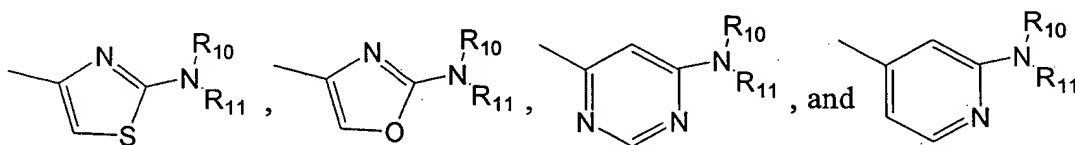
B is  $-S-$ ,  $-O-$ ,  $-CR^6=$  or  $-N=$ ,

Y is  $-CR^6=$  or  $-N=$ ,

Z is  $-CR^6=$  or  $-N=$ ; and

$n$  is zero or one.

14. (New) A compound according to claim 1 wherein  $R^3$  is selected from the group consisting of



15. (New) A compound according to claim 1 wherein

D is  $-CR^6=$ ;

B is  $-O-$  or  $-S-$ ;

Y is  $-N=$ ; and

n is zero.

16. (New) A compound according to claim 1 wherein

D is  $-\text{CR}^6=$  or  $-\text{N}=\text{}$ ;

B is  $-\text{N}=\text{}$ ;

Y is  $\text{CR}^6=$ ; and

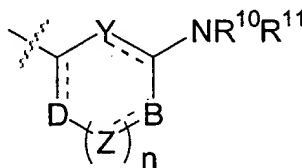
n is 1.

17. (New) A compound according to claim 1 wherein

$\text{R}^1$  and  $\text{R}^2$  are each independently selected from the group consisting of hydrogen, halogen, alkyl, and nitro;

$\text{R}^4$  and  $\text{R}^5$  are each independently selected from the group consisting of hydrogen and alkyl; and

$\text{R}^3$  is



wherein

D is  $-\text{CR}^6=$  or  $-\text{N}=\text{}$ ,

B is  $-\text{S}-$ ,  $-\text{O}-$ ,  $-\text{CR}^6=$  or  $-\text{N}=\text{}$ ,

Y is  $-\text{CR}^6=$  or  $-\text{N}=\text{}$ ,

Z is  $-\text{CR}^6=$  or  $-\text{N}=\text{}$ ; and

n is zero or one.

18. (New) A compound according to claim 1 wherein

$R^1$  and  $R^2$  are each independently selected from the group consisting of hydrogen, halogen, and haloalkyl; and

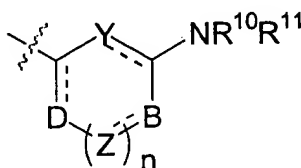
$R^4$  and  $R^5$  are each independently hydrogen.

19. (New) A compound according to claim 1 wherein

$R^1$  and  $R^2$  are each independently selected from the group consisting of hydrogen, halogen, and haloalkyl;

$R^4$  and  $R^5$  are each independently hydrogen; and

$R^3$  is



wherein

D is  $-CR^6=$  or  $-N=$ ,

B is  $-S-$ ,  $-O-$ ,  $-CR^6=$  or  $-N=$ ,

Y is  $-CR^6=$  or  $-N=$ ,

Z is  $-CR^6=$  or  $-N=$ ; and

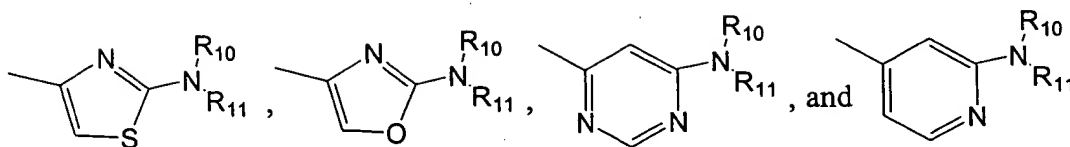
n is zero or one.

20. (New) A compound according to claim 1 wherein

$R^1$  and  $R^2$  are each independently are selected from the group consisting of hydrogen, chloro, and trifluoromethyl;

$R^4$  and  $R^5$  are each independently hydrogen; and

$R^3$  is selected from the group consisting of



21. (New) A compound according to claim 1 wherein R<sup>6</sup> is hydrogen.
22. (New) A compound according to claim 1 wherein
  - R<sup>1</sup> is selected from the group consisting of hydrogen, halogen and haloalkyl,
  - R<sup>2</sup> is selected from the group consisting of hydrogen and halogen, and
  - R<sup>4</sup> and R<sup>5</sup> are each independently hydrogen.
23. (New) A compound according to claim 22 wherein
  - R<sup>1</sup> is trifluoromethyl, and
  - R<sup>2</sup> is hydrogen.
24. (New) A compound according to claim 22 wherein R<sup>1</sup> and R<sup>2</sup> are each independently chloro.
25. (New) A compound according to claim 1 which has an IC<sub>50</sub> of less than 20  $\mu$ M when tested in one or both of
  - (i) an ICAM-1/LFA-1 Biochemical Interaction Assay, or
  - (ii) an ICAM-1/JY-8 Cell Adhesion Assay.
26. (New) A method for ameliorating a pathology in a mammal arising from the interaction of LFA-1 with ICAM-1 or ICAM-3 comprising administering to said mammal a therapeutic amount of a compound according to claim 1.
27. (New) A method according to claim 26 wherein the pathology is selected from an inflammatory disease, an autoimmune disease, tumor metastasis, allograft rejection and reperfusion injury.